DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 14, 2011 has been entered.

2. Claims 1 and 4-22 were previously pending. Applicants amended claim 1. Claims 1 and 4-22 are pending and will be examined.

3. Applicants' amendments did not overcome any of the previously presented rejections for reasons given in the "Response to Arguments" below.

Response to Arguments

4. Applicant's arguments filed January 14, 2011 have been fully considered but they are not persuasive.

A) Regarding the rejection of claims 1, 5-10, 14 and 16-28 under 35 U.S.C. 102(b) as anticipated by Smith et al., Applicants argue that:

"The amendment to claim 1 above clarifies that the nucleic acid that is filtered through the porous matrix used in the present invention is directly bound to the matrix. In contrast, Smith teaches use of an ion exchange matrix attached to a porous matrix support, whereby the nucleic acid attaches to the ion exchange matrix, not the porous matrix support. Thus, Smith does not teach or suggest the claimed invention."

However, this is not what the claims require. Step b) reads as follows:

" b) filtering the lysate through a porous matrix consisting of a material based on silica or of a silica coated material to bind the nucleic acid directly to the porous matrix in the absence of an alcohol and in the absence of a chaotropic salt".

The claims require silica coated material or material based on silica. Smith et al. matrix is a material based on silica, and the claims do not require that the DNA binds directly to the SiO groups.

The rejection is maintained.

B) Regarding the rejection of claims 4 and 19-22 under 35 U.S.C. 103(a) over Smith et al. and Colpan, Applicants argue as follows:

"Smith et al. does not teach binding of nucleic acids directly to a silica based or coated support and thus, even if one of skill in the art were to use the arrangement suggested by Colpan, the result would not be the present invention."

"The combination of Colpan and Smith et al. fails to disclose or suggest the present invention. First, Smith et al. teaches the use of an ion exchange matrix for binding the nucleic acids after disrupting the cells and does not disclose or suggest binding directly to the porous silica based or coated matrix. Second, Colpan teaches use of guanidine-HC1 in each instance where genomic DNA is the target of the isolation procedure. Thus, even if one were to combine the two cited references in the manner suggested by the Examiner, the result would not be the present invention where genomic DNA is released from cells in the absence of a chaotropic agent and captured by direct binding to a silica based or coated porous matrix."

The argument regarding Smith et al. reference was addressed above. Colpan is used to teach alternative form of silica-based material, namely, a membrane, and the fact that higher molecular weight DNA molecules can be successfully purified using silica-based material.

The rejection is maintained.

C) Regarding the rejection of claims 11-13 under 35 U.S.C. 1039a) over Smith et al., Applicants argue the following:

"As discussed above, Smith et al. does not disclose a filter system that binds DNA directly. Instead, Smith utilizes an ion exchange ligand attached to a solid support such as a silica bead. There is no teaching or suggestion that direct binding to the porous matrix can replace use of ion exchange resins. Thus, regardless of the size &the pores in the solid matrix, the invention of Smith et al. does not render the claimed invention obvious."

This argument was addressed above. The rejection is maintained.

D) Regarding the rejection of claim 15 under 35 U.S.C. 103(a) over Smith et al. and Heid et al., Applicants argue the following:

"The present invention differs from and is not rendered obvious by the teachings of Smith et al., alone or in combination with Heid et al. As discussed above, Smith et al. teaches use of a solid support porous matrix to which are attached pH dependent ion exchanges matrixes which bind nucleic acids from a cell lysate. The nucleic acid is not bound directly to the porous matrix as in the present invention. Heid et al. does not cure this deficiency in the primary reference."

The arguments regarding Smith et al. were addressed above.

The rejection is maintained.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1, 5-10, 14 and 16-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Smith et al. (U.S. Patent No. 6,310,199 B2; issued October 2001).

Regarding claim 1, Smith et al. teach a method of genomic DNA purification comprising:

a) lysing the nucleic acid source (col. 29, lines 46-52),

b) filtering the lysate through a porous matrix consisting of a material based on silica or of a silica coated material to bind the nucleic acid directly to the porous matrix in the absence of an alcohol and in the absence of a chaotropic salt (col. 25, lines 35-40; col. 29, lines 54-61; col. 8, lines 41-67; col. 9, lines 1-5; col. 10, lines 46-60; col. 14, lines 16-25 and 35-42),

c) eluting the nucleic acid from the porous matrix of step b) by using an aqueous buffer solution to provide isolated genomic DNA (col. 14, lines 16-25; col. 29, lines 63-65).

Regarding claims 5 and 6, Smith et al. teach blood, tissue, animal cells and bacteria (col. 1, lines 62-65; col. 7, lines 65-67; col. 23, lines 30-34; col. 29, lines 46-47).

Regarding claim 7, Smith et al. teach lysing solution which does not contain a chaotropic salt or alcohol (col. 14, lines 35-42; col. 29, lines 46-52).

Regarding claim 8, Smith et al. teach using proteinase K after cell lysis (col. 29, lines 54-55).

Regarding claims 9 and 10, Smith et al. teach silica and glass membranes (col. 8, lines 41-50; col. 10, lines 45-60).

Regarding claim 14, Smith et al. teach subsequent application of the DNA (col. 2, lines 58-59; col. 30, lines 1-5).

Regarding claim 16, Smith et al. teach centrifugation to eliminate cell debris (col. 23, lines 30-60).

Regarding claims 17 and 18, Smith et al. teach performing washes of matrix using washing buffer before eluting DNA (col. 29, lines 62-63).

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 4 and 19-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. (U.S. Patent No. 6,310,199 B2; issued October 2001) and Colpan (US 6,277,648 B1; cited in the previous office action).

A) The teachings of Smith et al. are presented above. They do not specifically teach genomic DNA in the size range between 10 and 50 kb or membrane filter plates or tubes.

B) Regarding claim 1, Colpan teaches a method of rapid isolation of nucleic acid, the method comprising:

a) lysing the nucleic acid source (col. 5, lines 3-5; col. 6, lines 34-36; col. 7, lines 4-6),

b) filtering the lysate through a porous matrix consisting of a material based on silica or of a silica coated material to bind the nucleic acid to the porous matrix in the absence of an alcohol and

in the absence of a chaotropic salt (col. 2, lines 1-8; col. 5, lines 8-18; col. 6, lines 41-52; col. 7, lines 13-18),

c) eluting the nucleic acid from the porous matrix of step b) by using an aqueous buffer solution (col. 5, lines 21-23; col. 6, lines 57-58; col. 7, lines 29-31).

Regarding claims 1 and 4, Colpan teaches genomic DNA and size range from 1 to 50 kb (col. 1, lines 65-67).

Regarding claim 19, Colpan teaches single column filter tube (Fig. 1-6).

Regarding claim 20, Colpan teaches multi-well filter plate 9col. 4, lines 58-62).

Regarding claim 21, Colpan teaches membrane assembled in multiple layers (Fig. 1).

Regarding claim 22, Colpan teaches pore sizes being different in the different layers (col. 2, lines 49-67).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the filter matrices of Smith et al. in the arrangement suggested by Colpan. The motivation to do so is provided by Colpan is that lysed cells were applied directly to filters without the need for centrifugation and cells could be lysed directly on filters (col. 1, lines 29-46; col. 5, lines 30-60).

5. Claims 11-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. (U.S. Patent No. 6,310,199 B2; issued October 2001).

Regarding claims 11-13, Smith et al. teach pore sizes larger than 0.6 microns (col. 10, lines 59-60), but do not specifically teach pore sizes in the range of between 0.2 and 3.2 microns.

However, it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have used filters with different pore sizes in the method of Smith et al. according to the size of DNA to be purified. It would have been prima facie obvious to perform

routine optimization to determine optimal filter pore size, as noted in *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the selection of specific filter pore sizes was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

6. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. (U.S. Patent No. 6,310,199 B2; issued October 2001) and Heid et al. (Genome Res., vol. 6, pp. 986-994, 1996).

A) Regarding claim 15, Smith et al. teach amplification of isolated DNA (col. 2, line 59), but do not specifically teach PCR or quantitative real-time PCR.

B) Heid et al. teach quantitative real-time PCR on human genomic DNA to determine a number of copies of a DNA gene (Abstract; page 987, third and fourth paragraph; page 988; page 993).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used real-time quantitative PCR of Heid et al. to analyze purified genomic DNA of Smith et al. The motivation to do so would have been that such analysis allowed for accurate quantitation of the amount of genomic DNA (see Fig. 1, for example). As stated by Heid et al. (page 991, last paragraph; page 992, first paragraph):

"The real-time PCR method offers several advantages over the other two methods currently employed (see the introduction). First, the real-time PCR method is performed in a closed-tube system and requires no post-PCR manipulation of sample. Therefore, the potential for PCR contamination in the laboratory is reduced because amplified products can be analyzed and disposed of without opening the reaction tubes. Second, this method supports the use of a normalization gene (i.e., [β-actin) for quantitative PCR or housekeeping genes for quantitative RT-PCR controls. Analysis is performed in real time during the log phase of product accumulation. Analysis during log phase permits many different genes (over a wide input target range) to be analyzed simultaneously, without concern of reaching reaction plateau at different cycles. This will make multigene analysis assays much easier to develop, because individual internal competitors will not be needed for each gene under analysis. Third, sample throughput will increase dramatically with the new method because there is no post-PCR processing time. Additionally, working in a 96-well format is highly compatible with automation technology."

7. No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA E. STRZELECKA whose telephone number is (571)272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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